R E M A R K S

Applicant has amended the claims of the application to place the application in condition for allowance.

With respect to the sequence listing noted by the examiner to appear on page 32, applicant is unable to find the same.

SEQ ID NO 29 on page 34 of the specification refers to the combination of the binding sites A3 and A4. Thus, the sequences listed therein include the region 25-42 and the region 37-54. In other words, monoclonal antibody 21C10-1D10 binds to sites A3 and A4.

With respect to the term "polymer mimicking an artificial antibody" applicant offers the following definition:

A polymer mimicking an artificial antibody is a biomemetic receptor capable of binding a target molecule with similar affinity and specificity as an antibody. The technique that has achieved this goal of generating artificial macromolecular receptors is referred to as molecular imprinting of synthetic polymers. This process utilizes both functional monomers and cross-linking monomers that are co-polymerized in the presence of a target analyte (the imprint molecule). This process further entails the target molecule acting as a molecular template and is further used to direct the assembly of specific binders followed by polymerization. Functional monomers form a complex with the imprint molecule, and following polymerization, their functional groups are held in position by the highly cross-linked polymeric

structure which forms a molecularly imprinted polymer (MIP). Subsequent removal of the imprint molecule reveals binding sites that are complimentary in size and shape to the analyte. In this process, a molecular memory is introduced into the polymer, which is now capable of selectively rebinding the analyte similarly to a monoclonal antibody. The MIP can be recovered and used directly as an artificial immobilized antibody.

With respect to the term "phage displayed binding sites", the following definition is offered:

A phage display antibody is employed because of the structural complexity of monoclonal antibodies. In this regard, the production in bacteria of complete immunoglobulins (Igs) has not been successful. abAb fragments that retain full antigen-binding capacity has been the goal. Thus, active Fab (antigen binding fragment of antibodies composed of heterodimeric VH-CH1/VL-CL) and single chain FV(scFv) fragments expressed in E coli have been produced. Cloning of large collections of scFv and Fab genes in phage vectors has allowed the display of these recombinant antibodies on the capsid of filamentous phage. Phage displayed antibodies permit the in vitro selection of clones with distinct antigen binding specificities by multiple rounds of panning, which mimics the clonal expansion of B cells in vivo. The generation of large combinatorial libraries of Fabs and scFvs displayed on phage has been achieved. The engineering and specific selection of phage displayed antibodies has been used to

improve the binding and stability properties of the antibodies, and the expression of phage displayed antibodies in different bacterial hosts has also been achieved.

The references to Ye et al, Fernandez, and Haupt are submitted as further information with respect to the above definitions. A United States Patent and Trademark Office Form 8B is also enclosed.

The Examiner has rejected the claims prior submitted under 37 CFR § 112. It is believed that the new claims submitted will overcome the objections raised by the Examiner. In this regard, the Markush groups include the suggested language of the Examiner and the new claims define the sequences therein as comprising peptide analogues.

In addition, a new terminal disclaimer is enclosed, indicating the owner and the percentage of ownership.

The Examiner is also rejecting the claims under § 103 as being unpatentable over Moncada et al in view of Maier, Harlow and Lane, and Marsden et al or Nakane et al. The Examiner has stated the instant invention includes the feature of lack of a cross-reactivity of the eNOS and nNOS isozymes while recognizing human iNOS. Maier and Nakane et al as well as Geller et al teach that the capital C terminus of mouse and human iNOS are different. However, the Harlow and Lane reference, states that the c-terminus might be a place to choose when developing an immunogen and that the size of the peptide should be six amino acids in length.

Harlow and Lane, however, does not show a clear road map to making an antibody such as those developed by applicant. In this regard, applicant is filing a § 132 declaration indicating that this technique did not work in a series of experiments over a period of 2 ½ years. It is believed that applicant's monoclonal antibody is novel in that the section § 132 declaration should be considered as rendering applicant's invention unobvious from the prior art cited by Examiner.

A three month extension of time to respond to the action is requested and a PTO 2038 Form for the requisite fee is enclosed. Any credit or deficiency in the fee may be credited to deposit account # 50-3935.

It is believed that the claims as submitted are now in condition for allowance and the passing to issue of the application at an early date is earnestly solicited.

Respectfully submitted,

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TJB:amb

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